HGFA Is an Injury-Regulated Systemic Factor that Induces the Transition of Stem Cells into GAlert.

Journal: Cell Rep

Publication Year: 2017

Authors: Joseph T Rodgers, Matthew D Schroeder, Chanthia Ma, Thomas A Rando

PubMed link: 28423312

Funding Grants: Molecular regulation of stem cell potency

Public Summary:
The activation of resting stem cells in tissues of adult animals to give rise to functional progeny is a key step in initiating the process of tissue repair. We recently reported that resting stem cells can transition into a cellular state in which they have an increased functional ability to activate and participate in tissue repair. However, the precise molecular signals that induce this state have remained elusive. Here, we show that the tissue injury induces the cleavage of a blood-circulating growth factor by enzymes in the blood. The cleaved growth factor stimulates the activation of different stem and progenitor cells in tissue to participate in tissue repair. We further demonstrate that administering the cleaved form of this growth factor directly into animals is sufficient to induce the more potent state of stem cells throughout the body. This significantly accelerates the processes of stem cell activation and tissue repair. Our data suggest that factors that elevate the potency of stem cells will have broad therapeutic applications for regenerative medicine and wound healing.

Scientific Abstract:
The activation of quiescent stem cells into the cell cycle is a key step in initiating the process of tissue repair. We recently reported that quiescent stem cells can transition into GAlert, a cellular state in which they have an increased functional ability to activate and participate in tissue repair. However, the precise molecular signals that induce GAlert in stem cells have remained elusive. Here, we show that the injury-induced regulation of hepatocyte growth factor (HGF) proteolytic processing via the systemic protease, hepatocyte growth factor activator (HGFA), stimulates GAlert in skeletal muscle stem cells (MuSCs) and fibro-adipogenic progenitors (FAPs). We demonstrate that administering active HGFA to animals is sufficient to induce GAlert in stem cells throughout the body and to significantly accelerate the processes of stem cell activation and tissue repair. Our data suggest that factors that induce GAlert will have broad therapeutic applications for regenerative medicine and wound healing.